Commentary

Confounding by Socioeconomic Status in Epidemiological Studies of Air Pollution and Health: Challenges and Opportunities

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BACKGROUND: Despite a vast air pollution epidemiology literature to date and the recognition that lower-socioeconomic status (SES) populations are often disproportionately exposed to pollution, there is little research identifying optimal means of adjusting for confounding by SES in air pollution epidemiology, nor is there a strong understanding of biases that may result from improper adjustment.

OBJECTIVE: We aim to provide a conceptualization of SES and a review of approaches to its measurement in the U.S. context and discuss pathways by which SES may influence health and confound effects of air pollution. We explore bias related to measurement and operationalization and identify statistical approaches to reduce bias and confounding.

DISCUSSION: Drawing on the social epidemiology, health geography, and economic literatures, we describe how SES, a multifaceted construct operating through myriad pathways, may be conceptualized and operationalized in air pollution epidemiology studies. SES varies across individuals within the contexts of place, time, and culture. Although no single variable or index can fully capture SES, many studies rely on only a single measure. We recommend examining multiple facets of SES appropriate to the study design. Furthermore, investigators should carefully consider the multiple mechanisms by which SES might be operating to identify those SES indicators that may be most appropriate for a given context or study design and assess the impact of improper adjustment on air pollution effect estimates. Last, exploring model contraction and expansion methods may enrich adjustment, whereas statistical approaches, such as quantitative bias analysis, may be used to evaluate residual confounding. https://doi.org/10.1289/EHP7980

Introduction

Studies in the United States and elsewhere have reported that long-term exposures to air pollution (AP) are associated with increased risk of all-cause (Dockery et al. 1993; Laden et al. 2006; Pope et al. 1995) and cause-specific mortality (Brook et al. 2010; Brunekreef et al. 2009; IARC 2013; Pope et al. 2002), as well as a host of other health outcomes [from cardiovascular disease (Brook et al. 2010) to cancer (IARC 2013) and depression (Fan et al. 2020)] across the life span [from childhood asthma (Khreis et al. 2017) to dementia (Power et al. 2016)]. Drawn mostly from the environmental justice literature, abundant evidence indicates that populations with lower socioeconomic status (SES) are more likely to be exposed to higher levels of air pollution than are those with higher SES (Brulle and Pellow 2006; Hajat et al. 2015; Miao et al. 2015; Mohai et al. 2009); this observation is also known as differential exposure in the social production of disease model by Diderichsen et al. (2001). Such findings, coupled with the consistent observation that the poor have worse health, have made it a common practice for AP epidemiology studies to adjust for SES, though questions remain about how accurate this confounding adjustment has been. In particular, the extent to which insufficient adjustment for socioeconomic factors might result in residual confounding of the association between AP and health effects. Researchers have responded with more extensive and more sophisticated analyses considering not only individual-level socioeconomic indicators but also neighborhood- and city-level indicators; see, for example, Krewski et al. (2009).

In addition to being a *confounder* of the AP–health association, evidence indicates that SES may be an important *effect modifier*, i.e., there is differential susceptibility across population subgroups (Diderichsen et al. 2001). Studies show that associations between AP and health outcomes are stronger in groups with lower SES (Bell et al. 2013; Clougherty et al. 2014; Fuller et al. 2017; Rodriguez-Villamizar et al. 2016; Vinikoor-Imler et al. 2014). Such results suggest that *not* examining effect modification may lead researchers to incorrectly estimate the true burden of air pollution. Finally, air pollution may be a *mediator* of SES effects on health, in that lower-income may lead to individuals living in less-expensive areas where land has been devalued (e.g., alongside major roadways or near industrial areas), increasing their exposures, consequently leading to disease. For purposes of this paper, however, although we acknowledge these other roles, we focus primarily on SES as a confounder in AP epidemiology studies.

Deciding how to account for the confounding effects of SES in any given study of AP health effects is challenging. SES is a multidimensional concept, capturing many dimensions of any individual's life over the life course and the myriad pathways through which material and psychosocial aspects of deprivation may affect health. Any of these dimensions may not be fully represented by any given measure and may differ by setting and across populations. Differences in measures used to define SES may account for some differences in findings between studies. For example, some studies where mortality was the outcome showed minimal confounding by socioeconomic factors (Chi et al. 2016; Di et al. 2017; Dockery et al. 1993; Krewski et al. 2009; Pope et al. 2002), whereas others have found substantial differences in effect estimates after adjustment for SES in one form or another (Jerrett et al. 2005; Krewski et al. 2009; Zeger et al. 2008). Specifically, in some studies there was a less than 5% difference in hazard ratios comparing models with and without several individual- and area-level SES measures representing multiple domains (Chi et al. 2016; Di et al. 2017; Dockery et al.

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1993; Krewski et al. 2009; Pope et al. 2002) but between 7% and 15% difference in ratio measures of effect for others (Jerrett et al. 2003; Krewski et al. 2009; Zeger et al. 2008). For example, Jerrett et al. found that the relative risk for the association between total suspended particulates and premature mortality was attenuated from 1.30 to 1.13 after adjustment for percent of families with low income (Jerrett et al. 2003). Zeger et al. found that the percentage increase in mortality rate per $10 \, \mu g/m^3$ higher $PM_{2.5}$ went from 17.8% to 8.9% after adjustment for five zip code−level SES variables (Zeger et al. 2008). It is notable that even after adjustment for SES there was still evidence of an effect of AP on mortality. Differences in study design, correlation between SES and AP of interest, the level at which SES is measured (e.g., individual, census tracts, zip codes, etc.), modeling approaches, and study populations, however, may also explain differing findings across studies.

Focusing on the role of SES as confounder, the primary goals of this paper are to: *a*) provide an overview of the conceptualization and measurement of factors used to represent SES in studies in the U.S. setting; *b*) describe pathways through which SES influences health and discuss factors that may create bias in AP effect estimates when adjusting for SES; and *c*) identify statistical approaches for addressing bias and confounding by SES in AP epidemiology. Furthermore, we focus primarily on studies of long-term AP. Although studies of acute health outcomes examining short-term exposure to AP are critical, most study designs for short-term (acute) impacts of AP (e.g., time-series, case-crossover) inherently control for non−time-varying covariates, including individual- and neighborhood-level SES, by virtue of comparing individuals or communities to themselves. Ultimately, because epidemiological studies are often used to inform regulation and policy, a better understanding of the role of SES is critical toward designing AP studies that may best inform public health and decision-making.

Discussion

SES has been variously defined by different academic disciplines as "refer[ing] to the social and economic factors that influence what positions individuals or groups hold within the structure of a society" (Galobardes et al. 2006b) or "a construct that reflects one's access to collectively desired resources..." (Oakes and Rossi 2003). The sociological literature has used the terms SES, social class, social status, and social stratification, all with distinct meanings. In the biomedical and public health literature the terms most commonly used are socioeconomic status (SES) and socioeconomic position (SEP), which are often used interchangeably (Berkman and Macintyre 1997; Oakes and Andrade 2017). Krieger et al. (1997) advocated for the use of "SEP," arguing that SES "blurs distinctions between two different aspects of socioeconomic position: (a) actual resources, and (b) status, meaning prestige—or rank-related characteristics," Oakes and Rossi (2003), however, disagree and propose a conceptualization of SES that consists of three domains: material (income and other goods), human (skills, ability and knowledge), and social capital (an individual's social network and the status it confers), similar to Bourdieu types of capital (Bourdieu 1986). Whereas resolving the definition of SES is beyond the scope of this manuscript, we aim to identify the domains that could influence one's exposure to AP as well as health—and how one may reasonably measure and account for these in studies of AP effects on health.

Indicators of Socioeconomic Status

Given the multidimensionality of SES, identification of a single indicator with a constant meaning and interpretability across all study questions and populations is not possible, nor of interest. Instead, we provide an overview of some of the most commonly used indicators in U.S. research relevant to epidemiological assessment of AP and health. Table 1 provides information about measurement and issues to consider when using these SES indicators. We do not believe that measurement of and adjustment for all of these variables are necessary to provide reliable estimates of the associations between AP and health outcomes. Investigators must consider these measures in the context of the particular exposures, health outcomes, and populations under study to determine whether measurement and adjustment are necessary.

Economic resources: income, poverty & wealth. In comparison with other indicators of SES, several studies showed that differential exposure to AP is greater for economic indicators (i.e., income and poverty) than indicators of education and occupation (described below) (Brochu et al. 2011; Clark et al. 2017; Rosofsky et al. 2018; Su et al. 2011). Households with higher incomes generally have the resources to live in areas with lower levels of AP and with overall better environmental quality. Higher income generally affords better-quality housing, which can reduce environmental exposures owing to both housing structure (e.g., indoor air quality) and location (e.g., near-highway air quality) (Graves et al. 1988) and may increase access to political capital to influence siting of AP sources (Mohai and Saha 2015). Investigators may consider individual or neighborhood levels of income, or other surrogates, such as measures of housing, material, and food insecurity (Rhee et al. 2019).

Few AP studies have examined associations with wealth. Wealth can be defined as total financial resources amassed over a lifetime (e.g., homes, stocks and bonds, etc), not just a flow of resources over a specific period of time (i.e., income) (Cubbin et al. 2011). Investigators may use wealth as a better indicator of SES than income, particularly in studies of chronic exposures and health outcomes in older populations, in which income is often lower due to retirement or unemployment and may not accurately capture an individual's financial resources. Wealth is, however, difficult to measure, requiring several questions quantifying dollar values on different types of assets and debts (e.g., home values, retirement funds, vehicles) (Cubbin et al. 2011). Kravitz-Wirtz et al. (2016) found a stronger association between home ownership (i.e., whether one rents vs. owns) and AP ($PM_{2.5}$, fine particulate matter with aerodynamic diameter less than 2.5 μm; and NO_2) compared with income and employment, whereas Hajat et al. (2013) found a moderate association between median home values and NO_x but no association with $PM_{2.5}$. Although housing values and home ownership comprise two aspects of wealth, it is possible that a more robust measure of wealth could be differently associated with AP. As with income, more wealth can mean lower environmental exposures via better housing, and more power to prevent undesirable land uses (highways, polluting facilities) from locating in wealthy communities.

Education. In some studies, differential exposure to AP by level of education has been shown to be greater than for income, poverty or wealth (Hajat et al. 2013; Zou et al. 2014). Education has been associated with cleaner communities and other health-promoting behaviors (e.g., better diet quality, nonsmoking, moderate alcohol consumption) (Ross and Wu 1995). Given education's role in improving social and material capital, education also works indirectly through other indicators of SES (income, wealth) to improve economic resources and enhance power and privilege (Elo 2009), ultimately reducing a person's exposure to AP and/or improving health. Refer to Table 1 for considerations when using education as an indicator of SES.

Occupation. Occupational status has been used as an indicator of SES in health studies. In a classic study, Rose and Marmot

Table 1. Indicators of socioeconomic status in U.S. context: descriptions and issues to consider.

SES indicator	Measurement at individual level	Measurement at contextual level	Measurement issues to consider	References[a]
Income	Captures household income as an absolute amount not as a range; account for family size to create equivalized (per capita) income measures	Usually a compositional variable, where individual incomes are summed over an area, e.g., median household income	Varys by time and by place; subject to both short and long-term fluctuations	Duncan et al. (2002)
Poverty	-Poverty threshold defined as above or below poverty line -Poverty level expressed as percentage of threshold (such as the federal poverty level)	Compositional variable: percent of households below poverty threshold	Varys by time and by place	Sen et al. (2006)
Wealth	Captures different types of asset (home values, stocks/bonds, pension/retirement accounts, savings accounts, etc.) and subtracts debt	Compositional variable such as median home values	Less impacted by short-term fluctuations; may be stable across generations (due to inheritance); better for older populations who no longer earn income	Cubbin et al. (2011)
Education	Can be specified as total years of education or highest degree obtained	Compositional variables: percent with a high school education, high school dropout rate, mean test scores	Varys by time (value of education has changed over time; e.g. a high school degree in 1960 creates more opportunity than a high school degree in 2010) and place (quality of education varies regionally)	Ross and Mirowsky (1999)
Occupation	Can be specified by occupation or industry or as employment status (e.g., employed, unemployed or not in the labor force)	Compositional variables: percent unemployed or not in the labor force, percent with managerial/professional occupation or percent with service occupation	Downstream of income and education Occupation and industry measures do not capture people not in the labor force or those who are temporarily unemployed	Ahonen et al. (2018)
Income inequality	NA	Range in incomes across a population in a given area, measured as a contextual (area-level) variable.	Several measures: including Gini Coefficient, Robin Hood Index, 20% share, Atkinson Index, and Concentration Index. Selection of geographic unit is important (e.g., counties vs. states)	De Maio (2007)
Subjective social status	Respondent's rating of social standing relative to others in their community, nation, etc.	Unaware of area-level equivalent	One commonly used measure shows a picture of a ladder and asks participants to place themselves on the rung where they believe they stand	Adler et al. (2000)
Composite SES indicator	SES indices usually derived from multiple SES indicators, either constructed by PCA or summed by assigning points to each indicator	SES indices usually derived from multiple SES indicators and constructed by PCA, commonly constructed for contextual-level analysis and referred to as area deprivation indices	-May be more statistically and conceptually efficient -Useful when individual SES indictors are highly correlated -Weighted indices (using weights from PCA) is recommended -Varies by space and time	Messer et al. (2006)

Note: NA, not applicable.
[a]References provide more information on conceptualization, and measurement, of SES.

(1981) demonstrated a consistent gradient in health for numerous disease outcomes according to occupational status. Occupation, particularly in industrial settings, can be an additional source of exposure to air pollutants and other physical and chemical hazards that could confound effects of ambient pollution on health (Siemiatycki et al. 2003; Tetreault et al. 2013). For example, although some manufacturing and professional workers may earn similar incomes, adjustment for occupation may help control for differences that are not fully controlled by income and education alone. A single occupation variable may not be adequate to control for confounding; Krewski et al. (2009), in their study of AP and mortality, included seven variables to characterize each subject's main lifetime occupation and his or her possible exposure to PM in the workplace, noting that many individuals change occupations or workplaces many times over the course of their careers. Occupational status results in differential susceptibility to AP's impacts on health, as shown in several acute (Katsouyanni et al. 2009; Samoli et al. 2008; Vinikoor-Imler et al. 2014) and long-term studies (Chi et al. 2016; Dockery et al. 1993). Whether

as a source of co-exposures or as an indicator of SES, occupation may either confound or modify AP's effects on health (Fuller et al. 2017; Siemiatycki et al. 2003) and, we believe, deserves further consideration in AP epidemiology studies.

Income inequality. Income inequality has been shown to affect population-level health outcomes negatively and is hypothesized to operate via both material and psychosocial pathways (Lynch et al. 2004; Pickett and Wilkinson 2015). Income inequality is an inherently aggregate-level variable (i.e., a characteristic of the place, not of any specific individual in that place). In contrast, most of the indicators discussed previously are conceptualized at the individual level (e.g., income) even if the only available proxy for a given study is aggregated (e.g., median income for a census tract).

The impact of income inequality will depend on an individual's own characteristics in relation to the distribution of income across the group. This phenomenon, referred to as "cross-level interaction" points to the complexities in attempting to adjust for confounding using these aggregate-level measures (Blakely and

Woodward 2000); aggregate measures may be more suited to effect modification using hierarchical analyses, where there is interest in understanding health effects for the individual within a given (social) context. Although few studies have examined differential susceptibility by income inequality, mounting evidence suggests higher inequality magnifies the negative effects of AP on life expectancy (Hill et al. 2019; Jorgenson et al. 2020). Similarly, only a few AP studies have adjusted for measures of income inequality as a means to control for confounding showing minimal to moderate bias (Jerrett et al. 2005; Krewski et al. 2009). Several economists have evaluated associations between income inequality and AP and have found mixed results; higher income inequality in some cases was associated with better (Voorheis 2016) and in other cases worse environmental quality (Heerink et al. 2001). Income inequality may also be perpetuating and maintaining inequity in AP distributions, thereby contributing to environmental health disparities.

Subjective measures of SES. To our knowledge, subjective measure of SES (i.e., perceptions of one's social standing relative to others) have not been used in AP and health studies to adjust for confounding, to evaluate differential exposure to AP or to assess differential susceptibility, in part because such metrics are not commonly available for large population-based studies. Subjective measures (e.g., MacArthur ladder), however, are used in other health literatures, including psychology (Adler et al. 2000) and social epidemiology (Wolff et al. 2010). In most AP epidemiology studies, however, subjective measures could help to capture important nonmaterial aspects of SES—i.e., dimensions of SES related to status or prestige, which are not fully reflected in measures of economic resources alone because, as mentioned previously, the meaning that material wealth confers varies across setting and culture.

Composite indicators of SES. Given the multifaceted nature of SES, and the limited statistical power in many epidemiological studies, investigators may develop a composite measure or index, collapsing many measures into one variable (Chan et al. 2015). Individual-level SES composite indices are less common in the AP literature due to the limited number of individual-level SES indicators collected by most observational AP epidemiology studies. Moreover, individual-level composite measures have lost favor outside the AP literature as studies have become more interested in specific mechanisms by which SES causes disease and because some indices have not been updated to reflect changes in occupational structure (Galobardes et al. 2006a; Rehkopf et al. 2016). On the other hand, area-level composite indicators, often known as "deprivation indices," are often used to quantify the SES of a neighborhood or other geographic area; the number of SES indicators provided by the U.S. Census make it a good source for creating small-area SES indices (Diez-Roux et al. 2001; Kind et al. 2014; Messer et al. 2006).

Composite measures may be more statistically efficient and conceptually appealing; they collapse multiple SES variables and arguably create a more holistic measure of SES (Galobardes et al. 2006a). Many studies of differential exposure have used composite indicators of SES; some have reported stronger associations of AP with an SES index in comparison with individual indicators alone (Rissman et al. 2013). Others find similar magnitudes for SES indices in comparison with individual indicators of poverty, income, education, or occupation (Hajat et al. 2013; Humphrey et al. 2019).

Indices can be created via principal components analysis (PCA) or another form of dimension reduction, in which weights for each indicator are used to form a composite measure. Investigators may also use unweighted indices, but these are often of poorer quality (Erqou et al. 2017) because there is little empirical or theoretical evidence to suggest that the many different aspects of SES or disadvantage should equally and strictly additively affect health. Likewise, indices constructed without a theoretical or empirical grounding for indicator selection are unlikely to be able to accurately adjust for confounding by SES. Area-level SES indices may differ depending on the population of interest; for example, indices developed specifically for children, such as the Child Opportunity Index, use data from multiple sources to create a comprehensive multidimensional index that seeks to capture factors that specifically affect healthy child development (Acevedo-Garcia et al. 2014).

Indices can have some disadvantages relative to individual SES measures, even when well-constructed. Collapsing multiple aspects of SES into a single variable may result in poorer performance either because the summary measures was developed in a population substantially different from the one under study or because the summary measured did not adequately capture the relationships between variables (Diez Roux 2007). However, there is some evidence in other settings that summary measures may generally work well (Austin et al. 2015). Indices may also be less comparable across studies, given their greater requirements for consistency in data availability and measurement of individual metrics across populations, time periods, or geographic locations (Krieger et al. 1997; Messer et al. 2006).

Effect Modification by SES in AP Epidemiology

Although effect modification by SES (i.e., differential susceptibility) is not the primary focus of this paper, it is important to address here in brief. Effect modification by SES is an area of growing importance in AP epidemiology, given substantial observed differences in susceptibility across population subgroups, with bearing on health disparities and effective allocation of pollution-reducing interventions. SES has been shown to act as an important modifier of AP effects on health. For example, the Harvard Six Cities Study reported higher rates of mortality among people with lower levels of educational attainment (Dockery et al. 1993). This finding has been repeated for many different air pollutants and health outcomes (Bell et al. 2013; Clougherty et al. 2014; Fuller et al. 2017; Rodriguez-Villamizar et al. 2016; Vinikoor-Imler et al. 2014). These results suggest that failure to examine susceptible subpopulations risks missing critical impacts of AP in those populations and/or underestimating its true effect.

Although many studies have found that lower-SES individuals and communities have greater susceptibility (stronger pollution–disease associations), this directionality has not been consistent in all studies (Krewski et al. 2009). These inconsistencies may be due to differences in the SES indicators used or in the relative distribution of SES among the individuals represented in any given cohort (especially when comparing cohorts across very different countries or communities), or they may be due to nonlinearities in susceptibility, including potential threshold and/or saturation effects (Clougherty and Kubzansky 2009).

In addition, many researchers have explored the role of psychosocial stress, an important product of life in many lower-SES settings, as an effect modifier of the AP–health association (Clougherty et al. 2007; Clougherty and Kubzansky 2009; Fuller et al. 2017). Chronic stress—shown to influence immune, endocrine, metabolic, and epigenetic pathways (McEwen 2017; Snyder-Mackler et al. 2016)—has been associated with a broad suite of outcomes, including many with well-established associations with AP (i.e., respiratory and cardiovascular disease). Poverty and low SES at both the individual and neighborhood levels are often considered sources of psychosocial stress (Miller et al. 2009; Rohleder 2014), blurring the distinction between SES and stress. Other potential sources of psychosocial stress, such as violence, perceived discrimination, perceived stress (often measured with the perceived stress scale)

(Cohen et al. 1983), and stressful life events (e.g., death, divorce) have all been examined as effect modifiers in AP epidemiology studies; however, evidence of effect modification by psychosocial stressors is mixed (Clougherty et al. 2007, 2014; Fuller et al. 2017, 2019). Social capital and social support are similar to stress, in that they are potential modifiers of the AP–health association; however, they may provide a source of resilience, not risk (Wang et al. 2018). In addition to the considerations noted above for selecting SES indicators, the psychosocial stress indicators selected should reasonably capture variance in stress experience across the population under study (Shannon et al. 2020).

Much of the recent work in this area is motivated by an interest in understanding which populations are most vulnerable to the health impacts of AP. The so-called "double jeopardy" hypothesis provides one explanation for why low-SES populations would be more vulnerable to the health effects of AP (Institute of Medicine Committee on Environmental Justice 1999; Morello-Frosch and Shenassa 2006). The double jeopardy hypothesis is based on two empirical observations. First, low-SES individuals and communities often face higher exposure to AP and other environmental hazards, i.e., differential exposure (Brulle and Pellow 2006; Hajat et al. 2015; Miao et al. 2015; Mohai et al. 2009). It should be noted that this gradient is most consistently found in the United States (Clark et al. 2014, 2017), but in European cities patterns of differential exposure tend to be more city-specific, with economically vibrant cities actually showing higher exposure among well-to-do populations (Fairburn et al. 2019; Padilla et al. 2014). Second, lower-SES individuals, in addition to having fewer resources, have several co-occurring risk factors, such as increased psychosocial stress, fewer opportunities for health-promoting behaviors, and less access to high-quality health care (Adkins et al. 2017; Brady and Matthews 2002; Haviland et al. 2005). In addition, lower-SES populations may have less access to "assets" or protective factors (such as green space, social capital, good-quality housing) that may help deflect the deleterious impacts of higher exposure to AP. These factors contribute to the increased vulnerability of low-SES populations to the negative health effects of AP (Clougherty et al. 2014; Fuller et al. 2017). Additional discussion of considerations for effect modification can be found in reviews dedicated to this topic (Clougherty et al. 2014; Fuller et al. 2017; Laurent et al. 2007).

Other Important Considerations in Measuring and Modeling SES

Issues of scale: individual-level vs. neighborhood-level SES. The SES variables discussed above may be measured at either the individual-level SES (ISES) or the area- or neighborhood-level SES (NSES). NSES may be subjective to definitions of neighborhood, defined by the local community (Ou et al. 2018), or to administrative delineations, such as a census tract, census block, or zip code. Although NSES has generally displayed stronger associations with AP (Cesaroni et al. 2010; Goodman et al. 2011; Hajat et al. 2013; Krieger et al. 2014), ISES has generally displayed stronger associations with health (Boylan and Robert 2017; Foraker et al. 2019). The relatively stronger NSES-AP association may be due to similar underlying root causes (e.g., power and privilege, or lack thereof), which determine neighborhood social and economic resources as well as other relevant environmental factors (e.g., land use). NSES and AP may also, in some cases, operate at similar spatial scales and thus may be more strongly correlated.

The relation between ISES and AP may work through multiple pathways. Pollution sources are often differentially located in low-income communities (Mohai and Saha 2015); even within low-income communities, those homes alongside large emitting sources (e.g., highways or industry) may be relatively less valued (Larsen and Blair 2014; Li and Saphores 2012). As such, there is

likely variation in AP exposure both between and within communities, correlated with NSES and ISES, respectively, prompting the need to adjust for both to achieve unbiased estimates of the association between AP and health.

Measures of ISES and NSES, although correlated, can capture different constructs either of an individual's vulnerability to or potential for exposure to AP. In general, NSES characteristics are not sufficient proxies for unmeasured ISES; they generally capture less variability than ISES, particularly where there is substantial ISES heterogeneity within the neighborhood (Diez Roux 2001, 2007; Galobardes et al. 2006a). For example, evidence suggests less geographic mobility by income among Black and Latinx populations who remain in lower-SES neighborhoods even after gaining higher incomes (de Souza Briggs and Keys 2009; South et al. 2005). Accordingly, ISES is also a poor proxy for NSES. Extensive research on neighborhoods and health has shown the importance of place above and beyond individual-level circumstances on a variety of health outcomes (Diez Roux and Mair 2010; Ruiz and Chaix 2019). Furthermore, measuring and adjusting only for NSES or for ISES may result in residual confounding; therefore, adjusting for both may help to alleviate this concern (Blakely and Woodward 2000; Hajat et al. 2015). Both ISES and NSES measures may be causally relevant to AP exposure and health outcomes and should be carefully considered in AP epidemiology studies.

The environmental epidemiology and exposure science communities have made great efforts in recent years toward vastly improving the spatial and temporal precision of AP exposure estimates for epidemiological research. These efforts have not been matched by a concurrent improvement in the precision with which SES factors are measured in studies of AP effects on health (Humphrey et al. 2019). It is important to recognize that AP and relevant SES measures may be operating at different scales from each other. AP is increasingly measured at small spatial scales (e.g., specific to an individual's geocoded address using fine-scale spatial models, for a specific day or hour of interest), whereas NSES may be measured at census tract or block, or crime may be measured at police precinct level, generally using annual-average rates.

This issue of differential spatial classification between SES and environmental exposures is important, in that each may truly operate at a different meaningful spatial scale (Humphrey et al. 2019); for example, many air pollutants follow a physical decay in concentrations going away from sources (i.e., concentrations reduce substantially within several hundred meters of a roadway) (Karner et al. 2010). Social factors, on the other hand, can vary at a "true" neighborhood scale (e.g., the neighborhood shares a common school district) or not [e.g., violence may vary tremendously within a neighborhood, and over time (i.e., by season)] (Clougherty and Kubzansky 2009; Diez Roux 2004). In geography, this mismatch between the scale of measurement and the "true" underlying spatial scale for a given phenomenon is referred to as the "uncertain geographic context" problem (Kwan 2012).

Outside densely populated urban cores, census tracts are often large and may be irregularly shaped. This spatial mismatch means that the NSES measures may very crudely approximate the spatial scale of AP. The population captured in a census tract, compared with the underlying grid of an urban pollution surface, is likely to be different, furthering concerns about the resolution of available SES measures matching that of the AP metric (Clougherty and Kubzansky 2009).

In terms of differential susceptibility, evidence suggests that both ISES and NSES modify the AP-health association (Fuller et al. 2017). Few U.S.-based papers examine effect modification by both NSES and ISES (Chi et al. 2016; Hicken et al. 2013); therefore, it is difficult to ascertain which level produces stronger effect modification. We suggest that investigators articulate the

rationale behind measuring variables at a certain scale and seek measures at the most meaningful scale possible. Multilevel or hierarchal models are a particularly useful tool when exploring effect modification especially if cross-level interaction (individual-level AP × NSES) is of interest.

Temporal changes in SES over the life course. Advances in life-course epidemiology have shown the importance of childhood SES in both early- and later-life health (Ben-Shlomo et al. 2016). It is important to use measures of SES that are most relevant to the stage of the life course of interest. For example, using parental education as a measure of early-life SES, and accumulated wealth as a measure of later-life SES, will better capture the access to resources that is relevant during those two very different life stages (Pollack et al. 2007). For chronic diseases with long etiologic periods, using SES measured earlier in time may capture a critical developmental period; measures of SES later in life may better capture the cumulative impacts of SES over time. Using SES measures at multiple time points may better adjust for SES in longitudinal settings but also may raise concerns about time-varying confounding. In addition, SES measures may undergo compositional changes (i.e., they mean different things at different times); for example, a high school degree in 1960 was more valuable (in terms of future earnings and wealth) than a high school education today, and it has become more a norm (rather than an exception) that young people obtain a bachelor's degree. Studies including people born over many generations (or cohorts) may consider standardizing measures over time (Dowd and Hamoudi 2014; Meara et al. 2008) or otherwise account for effects of education or other social factors for which there have been substantial shifts in social meaning (e.g., LGBTQ rights) in the context of secular trends.

In selecting SES measures for a study, care must be taken to identify the temporal scale relevant to the study design and hypotheses (Krieger et al. 1997); for example, where the interest is in evaluating the short-term impacts of AP (daily) on some health outcome, understanding the context of recent stressful events (e.g., daily variation in reported assaults) may provide better adjustment for confounding than using average crime rates over longer time periods, even though they may be more stable estimates. Such an approach would be relevant where there is interest in the acute effects of either exposure; questions related to chronic exposures and cumulative susceptibility would still require longer-term measures (Galobardes et al. 2006a).

Race and gender. Finally, we recognize that race, gender, and socioeconomic factors are distinct but tightly intertwined constructs, and each introduce additional complexities in understanding and adjusting for SES (Kaufman and Cooper 2001; VanderWeele and Robinson 2014). The complex effects of these features of individual identity would be obscured if investigators did not attempt to separately account for race, gender, and SES and the interactions therein (Bowleg 2012). The renewed focus on intersectionality, a theoretical framework for understanding how multiple social identities interact at the individual level to reflect structural privilege and oppression, may help address some of the conceptual and theoretical complexity inherent in incorporating these identities in population health research (Bauer 2014; Bowleg 2012). Capturing intersectional identities analytically remains challenging; however, as an active area of ongoing research, methods are currently being developed and tested (Bauer and Scheim 2019; Jackson et al. 2016; Jackson and VanderWeele 2019). We refer readers to a recent paper that examines the role of race in environmental epidemiology (Benmarhnia et al. 2021) and the frameworks for disentangling aspects of gender (socially derived roles and activities) from biological sex, with particular relevance to the distinction between environmental exposures (related to job roles, activity patterns, etc.) vs. biological susceptibility to environmental pollutants (Clougherty 2010).

Design and Statistical Methods to Adjust for Confounding by SES

Adequate adjustment for confounding in long-term AP studies generally requires that the confounding factors discussed above have been thoroughly measured in the data collection phase of the study. Adequately adjusting for a confounder in a cohort study requires that it must be measured with minimal misclassification at the individual, neighborhood, or other scale appropriate to the study. In common epidemiological practice, if an investigator believes SES could be an effect measure modifier of the AP–health outcome relation, they would stratify the results by SES, often categorizing SES (or use interaction terms in a regression model). At this point, residual confounding by SES within stratum could still be a concern. As the previous discussion suggests, measurement error in SES is difficult to eliminate entirely, which limits the ability of the investigator to control fully for confounding. If the measurement error in a confounder does not depend on either the exposure or the outcome of interest, then controlling for it will remove some confounding; the effect estimate will, however, still suffer from residual confounding from that variable (Lash et al. 2009; Rothman et al. 2008). For example, in a study of chronic $PM_{2.5}$ exposures on cardiovascular disease (CVD), a researcher might wish to adjust for income as a proxy for SES. If income is misclassified, but that misclassification does not depend on $PM_{2.5}$ or CVD, then adjusting for income will remove some, but not all, confounding by SES. Unfortunately, without information on the extent of misclassification, it is impossible to determine exactly how much confounding has been removed. Further, if the misclassification is conditional on either the exposure or the outcome, adjusting for that confounder could introduce additional bias, rather than removing any confounding (Lash et al. 2009).

Even assuming SES confounders are measured perfectly, investigators may still have concerns about the feasibility of fitting certain statistical models or approaches because of sparse data. Sparse data can occur for various reasons, and it is important for study investigators to carefully consider why these data patterns are observed. Sparse data can be conceptualized as having only a few (or even no) people in a cell of an exposure–outcome–confounder contingency table (Hamra et al. 2013), such as by having few high-SES/high-pollution neighborhoods represented in a given data set. Sparse data can also occur if there are highly correlated variables in the data set (MacLehose et al. 2007); because many of the SES indicators described above may be relatively highly correlated, attempting to include a large number of them in a single model may result in estimability problems (e.g., a regression model could fail to converge or estimate extremely imprecise effects). Statistical methods have been developed to analyze sparse data occurring because of a large number of confounders, high correlation between variables, or small sample sizes. These methods typically fit in one of two general categories: model contraction or model expansion, which will be discussed in more detail below.

A common approach is to contract (i.e., increase parsimony in) the regression model to allow the model to fit. More sophisticated model contraction methods combine measured confounders into a summary estimate, as discussed for SES indices above, such as principal components analysis (Messer et al. 2006). Although these summary measures may make models easier to fit and be somewhat easier to interpret (because there is only one summary SES measure), they also have limitations, noted in the discussion under "Composite indicators of SES." Machine learning algorithms, such as the elastic net and lasso, have seen increasing use in public health research (Tibshirani 1996; Zou and Hastie 2005). These algorithms automatically select which variables are included in a regression model, often based on their association with the outcome of interest. We caution, however, that, with some notable exceptions (Crainiceanu et al. 2008;

Wang et al. 2012), these methods may not be amenable to confounder selection, which should also depend on the association of the confounder with the exposure.

Alternatively, model expansion techniques (which allocate more degrees of freedom to SES adjustment variables, potentially allowing for a more flexible adjustment) allow investigators to include all possible confounders in the model, even in the presence of sparse data (Gelman and Hill 2007). Hierarchical, or multilevel, models are a common approach to achieve model expansion. There are many ways to implement hierarchical models to stabilize estimation in the presence of sparse data. In a Bayesian framework, a prior distribution can be placed on the effect of the confounder on the outcome. This prior distribution essentially adds a small amount of data to the regression model (Greenland 2007). Epidemiologists often use vague or weakly informative priors in this situation, such that their prior distribution do not overly influence results (Gelman et al. 2008). Similar (and sometimes identical) models may be implemented from a frequentist perspective through use of penalized likelihoods (Hoerl and Kennard 1970).

Hierarchical models may also be useful in adjustment of measured confounding when important sources of confounding occur at multiple levels (Gelman and Hill 2007). For instance, both individual income and neighborhood income could confound the effect of AP on health. Because these variables occur at different levels (individual vs. neighborhood), investigators will typically use a hierarchical model to account for the nesting of individuals within neighborhoods; these models are often necessary to produce correct standard errors (Diez-Roux 2000). Care must be taken when using hierarchical models in this way, however, because the correlation between individual and neighborhood income may be extremely high (i.e., there may be few, if any, poor individuals living in high-income neighborhoods, or wealthy individuals in low-income neighborhoods). Clustering by race or ethnicity may be even stronger than clustering by income. Oakes (2006) referred to this phenomenon as structural confounding, and it relates closely to the issues of sparseness and positivity discussed above (Messer et al. 2010). Careful tabular examination of the data is necessary to detect such problems.

Quantitative bias analysis. All epidemiological studies are subject to some residual bias (Rothman et al. 2008), regardless of how well they are conducted; the challenges represented by misclassification of SES variables and residual confounding by unmeasured SES variables discussed above are not unique to the AP epidemiology literature. What is important is that investigators explore, quantify, and report the potential for bias in their publications through sensitivity analyses, rather than to simply mention their possible existence (Lash et al. 2014).

Quantitative bias analysis methods for uncontrolled confounding and misclassification of confounding are well-established, simple methods to perform sensitivity analyses (Lash et al. 2009, 2014). These methods require a researcher to unambiguously specify the SES measure of concern and to specify values for the following bias parameters: the association between the unmeasured SES variable and AP, the association between the unmeasured SES variable and the health outcome, and the prevalence of the unmeasured SES variable. To the extent possible, investigators should rely on prior literature to specify these values (Lash et al. 2009). After specifying the bias parameters, investigators can use relatively simple formulae to estimate the effect that would have been estimated in the absence of that bias (Arah et al. 2008; Schlesselman 1978).

Conclusions and Recommendations

SES is a complex and multifaceted construct that can vary spatially and temporally. No single variable or index of multiple variables can fully capture its relevance in a particular study; nevertheless, we found that many studies rely only on single measures of SES (e.g., income or education level) and do not further explore the myriad pathways and measures through which SES may influence health and the observed pollution–health relationship.

We believe that investigators should begin with a clear conceptualization of the aspects of SES (e.g., material, social, and/or human, capital) that may be most important for the study question and use this conceptualization to underpin the practical and operational decisions of SES measurement. A better understanding of the possible mechanisms by which SES operates to affect the health outcome under study will help investigators to decide which SES metrics are most important for their study (Elo 2009). It may be the case, however, that investigators are unable to identify all of the many pathways plausibly affecting health. Therefore, we generally recommend adjusting for SES using multiple variables whenever possible. Experimenting with indicators from different domains (e.g., income, education) and including indicators from different geographic scales (e.g., individual and neighborhood) may help alleviate residual confounding. Ideally, SES variables should be specified with the most resolution and granularity possible and in a manner that captures as much variance as possible in epidemiologic models (i.e., continuous variables, nonlinear forms) (Humphrey et al. 2019).

Specifically, we recommend that investigators identify: *a*) which available SES measures may be most appropriate to the population under study, (e.g., young, old, specific race/ethnic group), including common co-exposures or risk factors in this population; *b*) which SES indicators have been most strongly associated with the health outcome of interest; *c*) which SES indicators have been shown to be both spatially and temporally associated with AP in that setting; and *d*) the correlations among candidate indicators of SES. If possible, a thorough empirical assessment of SES variables as done in Shmool et al. (2014) (i.e., examining correlations among a large set of SES variables, AP and health outcomes) can provide a clearer understanding of how best to adjust for SES in a given study.

Acknowledgments

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